Jenny trying to understand TREMBLE

me

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1. My Notes

I. Derivation of TREMBLE

When there is more than three compartments, the number of parameters becomes so large that regression analysis fails to fit accurate estimates. The analysis can be simplified to describe tracer accumulation into a precursor compartment, which contains exchangeable ligands, m_e^*, which affects the transfer of ligand to the subsequent compartments 1.1. The exchange of tracer from plasma to the precursor compartment can be described as follows,

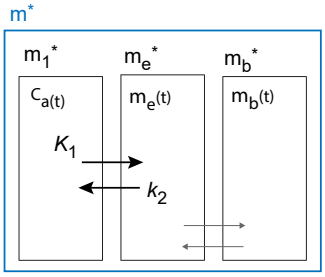

Figure 1.1

$$\frac{dm_1(t)}{dt} = V_0 \ \frac{dc_a(t)}{dt}, \tag{1.1}$$

where V_0 is the volume of the vascular bed, $c_a(t)$ is the time-variable concentration in plasma. The exchange of ligand from the precursor compartment to plasma is described as,

$$\frac{dm_e(t)}{dt} = K_1 \ c_a(t) - k_2 \ m_e(t), \tag{1.2}$$

combination of eqs. 1.1 and 1.2 yields the observed values, $m(t)$,

$$\frac{dm(t)}{dt} = V_0 \ \frac{dc_a(t)}{dt} \ + \ \Big(K_1 \ c_a(t) - k_2 \ m_e(t) \Big). \tag{1.3}$$

By rearrangement of eq. 1.3, the content of ligand in the exchangeable compartment can also be expressed as,

$$\frac{dm_e(t)}{dt} = \frac{dm(t)}{dt} \ - \ V_0 \ \frac{dc_a(t)}{dt} = K_1 \ c_a(t) - k_2 \ m_e(t) \tag{1.4}$$

$$\frac{1}{K_1} \left(\frac{dm(t)}{dt} \ - \ V_0 \right) = c_a(t) - \frac{k_2}{K_1} \ m_e(t) \tag{1.5}$$

$$\frac{k_2}{K_1} m_e(t) = c_a(t) - \frac{1}{K_1} \left(\frac{dm(t)}{dt} \ - \ V_0 \right) \tag{1.6}$$

$$m_e(t) = V_e \left[c_a(t) - \frac{1}{K_1} \left(\frac{dm(t)}{dt} \ - \ V_0 \right) \right], \tag{1.7}$$

where $V_e = K_1/k_2$ is the partition volume of exchangeable ligand (e.g. volume of distribution in cerebellum).

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Bibliography